

CLAIMS:

We Claim:

1. A pharmaceutical composition comprising a plurality of non-spherical granules, wherein said granules do not contain a coated core region and further comprise:
 - a. an antifungal active pharmaceutical ingredient;
 - b. a bulking agent;
 - c. a disintegrant;
 - d. a binding agent;
 - e. an acid; and,wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.
2. The composition of claim 1, wherein said composition is a pharmaceutically acceptable dosage form selected from the group consisting of tablet, capsule and caplet.
3. The composition of claim 1, wherein said antifungal active pharmaceutical ingredient is selected from the group consisting of itraconazole, saperconazole, ketoconazole, voriconazole and fluconazole.
4. The composition of claim 1, wherein said bulking agent is selected from the group consisting of mannitol and microcrystalline cellulose.
5. The composition of claim 1, wherein said disintegrant is selected from the group consisting of croscarmellose sodium, crospovidone, sodium starch glycolate.
6. The composition of claim 1, wherein said disintegrant comprises a mixture of croscarmellose sodium and crospovidone.
7. The composition of claim 1, wherein said binding agent is selected from the group consisting of polyvinyl pyrrolidone and polyvinyl pyrrolidone K25.
8. The composition of claim 1, wherein said acid is hydrochloric acid.
9. The composition of claim 1, wherein said non-spherical granules further comprise a cyclodextrin.
10. The composition of claim 9, wherein said cyclodextrin is hydroxypropyl- β -cyclodextrin.

11. The composition of claim 1, wherein said non-spherical granules further comprise a second disintegrant.
12. The composition of claim 11, wherein said second disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
13. The composition of claim 11, wherein said non-spherical granules further comprise a third disintegrant.
14. The composition of claim 11, wherein said third disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
15. A method for the treatment of fungal infections which comprises administering to a patient in need thereof an effective amount of a dosage form according to claim 1.
16. A pharmaceutical composition comprising a plurality of non-spherical granules, wherein said granules do not contain a coated core region and further comprise:
 - (a) itraconazole;
 - (b) a binding agent selected from the group consisting of mannitol and microcrystalline cellulose;
 - (c) croscarmellose sodium;
 - (d) polyvinyl pyrrolidone;
 - (e) and hydrochloric acid; and,wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.
17. A method for the treatment of fungal infections which comprises administering to a patient in need thereof an effective amount of a dosage form according to claim 16.
18. A pharmaceutical composition comprising a plurality of non-spherical granules, wherein said granules do not contain a coated core region and further comprise:
 - (a) itraconazole;
 - (b) a bulking agent selected from the group consisting of mannitol and microcrystalline cellulose;
 - (c) a croscarmellose sodium and crospovidone mixture;

- (d) crospovidone;
- (e) polyvinyl pyrrolidone;
- (f) a cyclodextrin; and
- (g) hydrochloric acid; and,

wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.

- 19. The composition of claim 18, wherein said cyclodextrin is hydroxypropyl- β -cyclodextrin.
- 20. A method for the treatment of fungal infections which comprises administering to a patient in need thereof an effective amount of a pharmaceutical dosage form according to claim 18.
- 21. A method for preparing a pharmaceutical dosage form including a plurality of non-spherical granules, wherein said granules do not contain a coated core region, comprising the steps of:
 - (a) dissolving an antifungal active pharmaceutical ingredient in an alcohol, an acid, and water;
 - (b) mixing a bulking agent, a disintegrant, and a binding agent to form a base mixture;
 - (c) granulating the mixture of step (b) with the mixture of step (a); and
 - (d) forming a pharmaceutical dosage form from the non-spherical granules from step (c); and,wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.
- 22. The method of claim 21, wherein said pharmaceutical dosage form is selected from the group consisting of tablet, capsule and caplet.
- 23. The method of claim 21, wherein said antifungal active pharmaceutical ingredient is selected from the group consisting of itraconazole, saperconazole, ketoconazole, voriconazole and fluconazole.
- 24. The method of claim 21, wherein said alcohol is ethanol.
- 25. The method of claim 21, wherein said acid is hydrochloric acid.

26. The method of claim 21, wherein said bulking agent is selected from the group consisting of mannitol and microcrystalline cellulose.
27. The method of claim 21, wherein said disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
28. The method of claim 21, wherein said binding agent is selected from the group consisting of polyvinyl pyrrolidone and polyvinyl pyrrolidone K25.
29. A method of treatment of fungal infections which comprises administering to a patient in need thereof an effective amount of a dosage form according to claim 21.
30. A method for preparing a pharmaceutical dosage form including a plurality of non-spherical granules, wherein said granules do not contain a coated core region, comprising the steps of:
 - (a) dissolving an antifungal active pharmaceutical ingredient in an alcohol, an acid, and water;
 - (b) adding a cyclodextrin dissolved in water to the solution of step (a);
 - (c) mixing a bulking agent, a first disintegrant, and a binding agent;
 - (d) granulating the mixture of step (c) with the solution of step
 - (e) adding a mixture of a second disintegrant and a lubricant to the mixture of step
 - (f) compacting the mixture of step (e) into a compacted mass;
 - (g) milling and sizing said compacted mass into non-spherical granules;
 - (h) adding a third disintegrant to said non-spherical granules; and
 - (i) forming a pharmaceutical dosage form from said non-spherical granules and, wherein said antifungal active pharmaceutical ingredients is distributed uniformly throughout the non-spherical granule.
31. The method of claim 31, wherein said pharmaceutical dosage form is selected from the group consisting of tablet, capsule and caplet.
32. The method of claim 31, wherein said antifungal active pharmaceutical ingredient is selected from the group consisting of itraconazole, saperconazole, ketoconazole, voriconazole and fluconazole.
33. The method of claim 31, wherein said alcohol is ethanol.

34. The method of claim 31, wherein said acid is hydrochloric acid.
35. The method of claim 31, wherein said cyclodextrin is hydroxypropyl- β -cyclodextrin.
36. The method of claim 31, wherein said bulking agent is microcrystalline cellulose.
37. The method of claim 31, wherein said first disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
38. The method of claim 31, wherein said disintegrant comprises a mixture of croscarmellose sodium and crospovidone.
39. The method of claim 31, wherein said binding agent is selected from the group consisting of polyvinyl pyrrolidone and polyvinyl pyrrolidone K25.
40. The method of claim 31, wherein said second disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
41. The method of claim 31, wherein said lubricant is magnesium stearate.
42. The method of claim 31, wherein said third disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium and sodium starch glycolate.
43. A method of treatment of fungal infections which comprises administering to a patient in need thereof a pharmaceutical dosage form according to claim 31.
44. A method for preparing a pharmaceutical dosage form including a plurality of non-spherical granules, wherein said granules do not contain a coated core region, comprising the steps of:
 - (a) dissolving itraconazole in ethanol, hydrochloric acid, and water;
 - (b) mixing a bulking agent selected from the group consisting of mannitol and microcrystalline cellulose, croscarmellose cellulose, and polyvinyl pyrrolidone;
 - (c) granulating the base mixture of step (b) with the solution of step (a); and
 - (d) forming a pharmaceutical dosage from the non-spherical granules of step (c) and,wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.
45. A method of treatment of fungal infections which comprises administering to a patient in need thereof a dosage form according to claim 44.

46. A method for preparing a pharmaceutical dosage form including a plurality of non-spherical granules, wherein said granules do not contain a coated core region, comprising the steps of:
- (a) dissolving itraconazole in ethanol, hydrochloric acid, and water;
 - (b) adding a cyclodextrin dissolved in water to the solution of step (a);
 - (c) mixing microcrystalline cellulose, a croscarmellose sodium and crospovidone mixture, and polyvinyl pyrrolidone;
 - (d) granulating the mixture of step (c) with the solution of step (b);
 - (e) adding a mixture of a crospovidone and magnesium stearate to the granules of step (c);
 - (f) compacting said granules into a compacted mass;
 - (g) milling and sizing said compacted mass into non-spherical granules;
 - (h) adding crospovidone to said non-spherical granules; and
 - (i) forming a pharmaceutical dosage form from said non-spherical granules; and, wherein said antifungal active pharmaceutical ingredient is distributed uniformly throughout the non-spherical granule.
47. The method of claim 46, wherein said cyclodextrin is hydroxypropyl- β -cyclodextrin.
48. A method of treatment of fungal infections which comprises administering to a patient in need thereof a dosage form according to claim 46.